Resident Conference: Thyroid Cases

Hypothyroidism and Thyroid Nodules

December 1999

Goals

- Review laboratory diagnosis of hypothyroidism
- Clinical consequences and management of subclinical hypothyroidism
- Overview of thyroid nodule diagnosis and management

Ask an Endocrinologist

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Mon, 13 Dec 1999 15:55:43 (#46)
Subj: weird thyroid tests Wed, 08 Dec 1999 14:45:20 7 Lines
From: RECENT GRADUATE (OUTSIDE CLINIC) 4 of 4 Responses read. in 'IN' basket.

A pt of mine (50s wf) has fibromyalgia, and is followed by civilian Rheum. Because she c/o fatigue, and thyroid dz runs in family, Rheum doc asked for some blood work. Pt asked me to put it in chcs for her. Well, I can't find and have never heard of a **FTI** and **T3RU**

Can someone enlighten me? It seems like a bit of a shot-gun for assessing fatigue

Case #1: 64-Year-Old Female

- Chief complaint
  - Increased fatigue after playing tennis
  - Weight gain despite exercise and diet
- History
  - Hypertension (155/95) for 5 years
  - Treated w/ diltiazem 180 mg/d
  - Postmenopausal on HRT
  - FH significant for brother w/ MI in 50s

Case #1: 64-Year-Old Female

Physical Examination

- BP 148/92 HR 58
- Height 5’8” Weight 190 lbs.
- Thyroid : difficult exam, no goiter
- Remainder of exam unremarkable

Case #1: 64-Year-Old Female

Laboratory

- CBC, electrolytes, LFTs, UA normal
- Cholesterol 265 mg/dL, HDL 42 mg/dL, LDL 190 mg/dL, TG 165 mg/dL
- CPK 247 (85-195), normal MB fraction

Case #1: 64-Year-Old Female

Treatment

- Continue diltiazem
- Add pravastatin 20 mg hs
- Follow-up in 6 weeks

Case #1: 64-Year-Old Female

- Six-Week Follow-up
  - Fatigue continues
  - BP 148/98
  - LDL 172
  - Diltiazem increased
  - TFTS sent

Case #1: 64-Year-Old Female

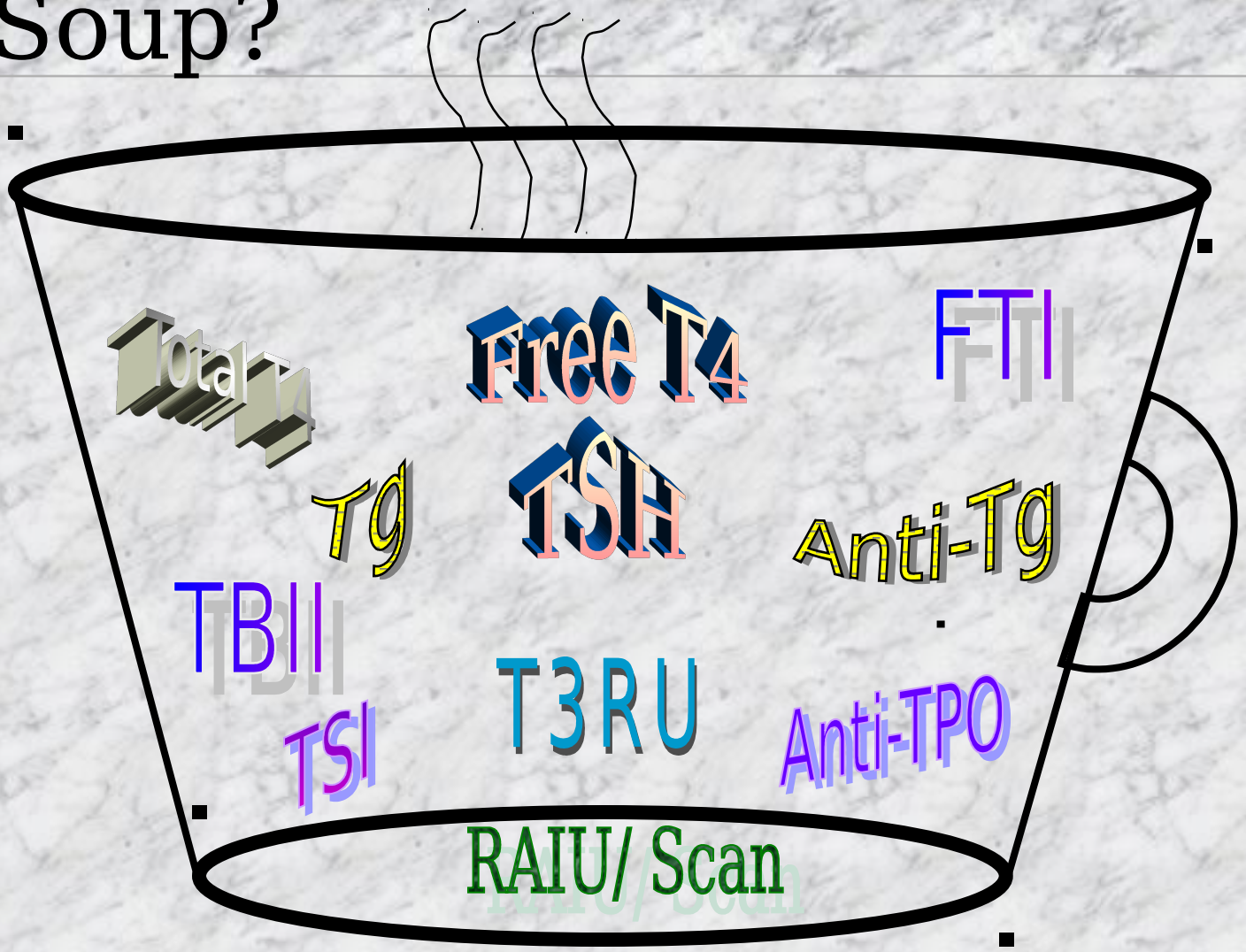
- Total T4 9.5 ug/dL (normal 4-11 ug/dL)
- T3RU 28% (normal 35-45%)
- FTI 1.8 (normal 1.75-4.6)
- TSH: 18 mIU/L (normal 0.5-5.0 mU/L)
- Anti-thyroid peroxidase 205 U/mL (normal 0-2 U/mL)

Case #1: 64-Year-Old Female

Questions:

- How would you interpret the thyroid function test results?
- What is the diagnosis?
- What treatment would you recommend?
- Will this treatment affect her BP and lipids?

Thyroid Lab Tests: TFT Soup?



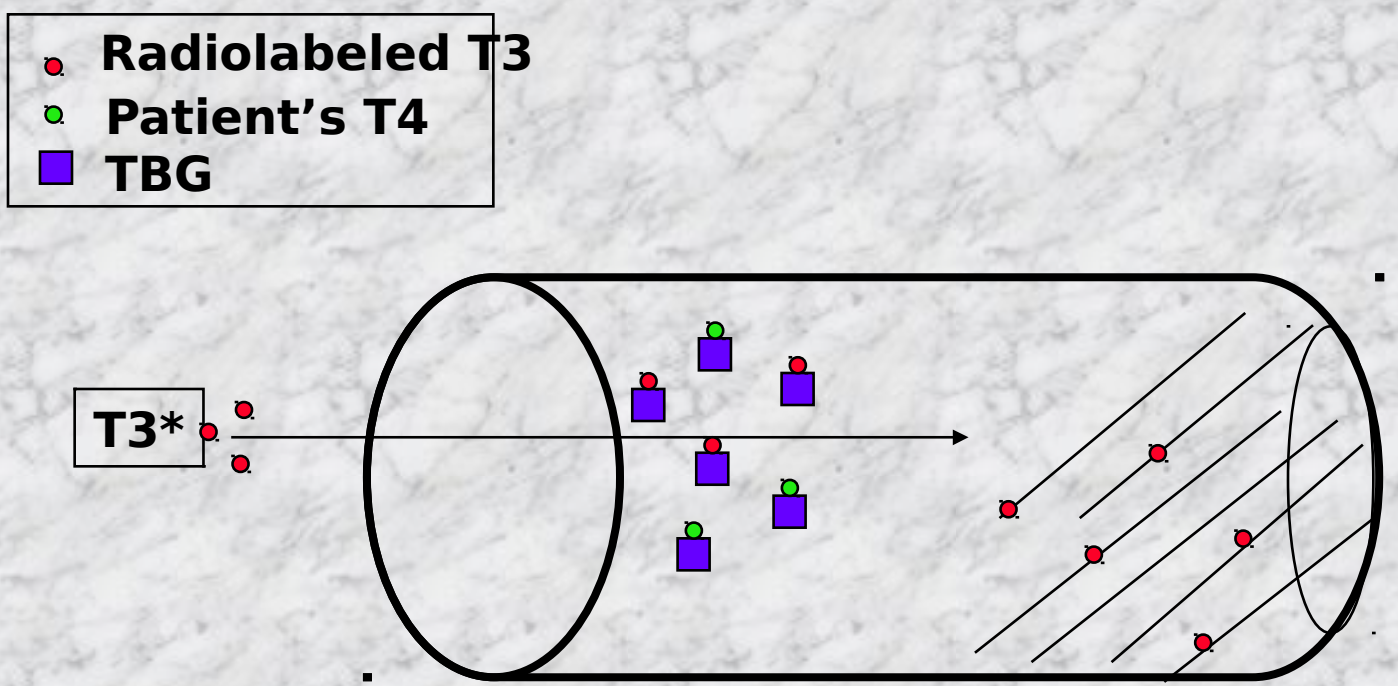
Weird Thyroid Tests

- Best single test to screen for hypothyroidism: TSH
- Best combination: TSH & Free T4
- Common substitutes for FT4:
  - Total T4, T3RU, FTI
- What are the FTI and T3RU??

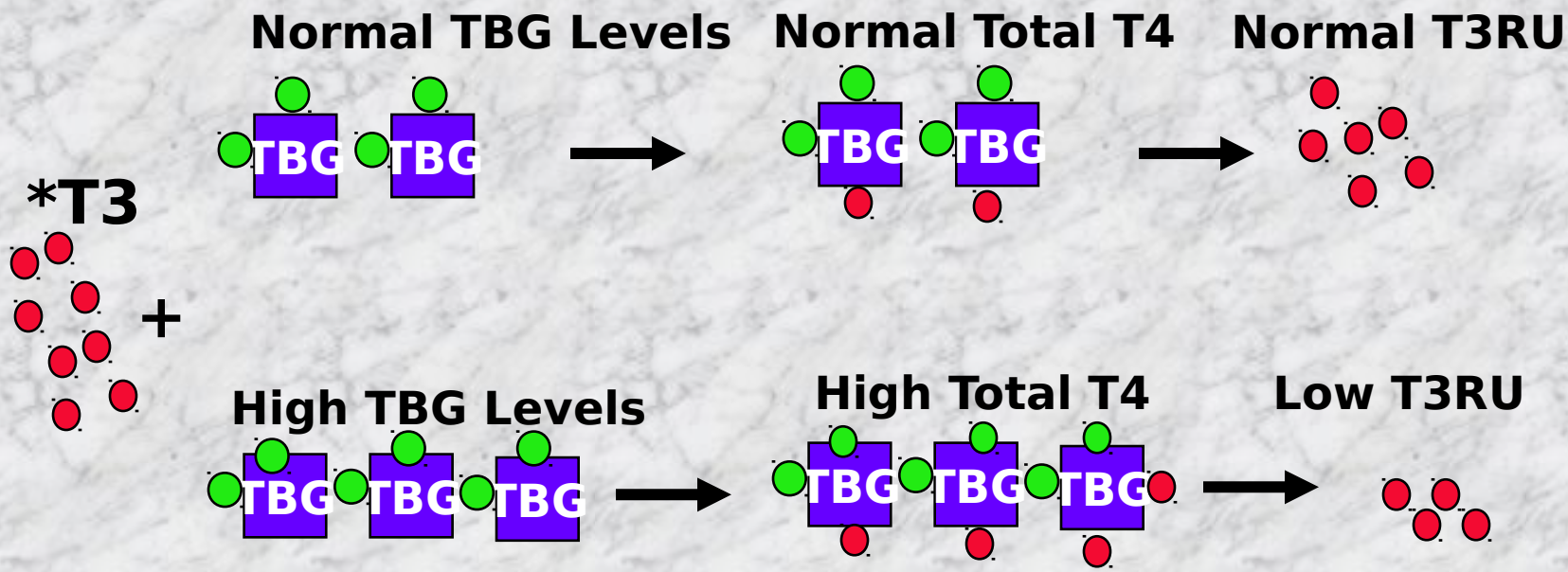
What is the FTI??

- FTI (Free Thyroxine Index) gives an estimate of the true Free T4 value
- FTI = Total T4 x T3RU x Constant
- T3RU accounts for alterations in thyroid hormone binding proteins (TBG, prealbumin, albumin)

What is the T3RU?



What is the T3RU?



FTI = Total T4 x T3RU

Case #1: 64-Year-Old Female

Questions:

- Interpret the thyroid function test results.
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- What treatment would you recommend?
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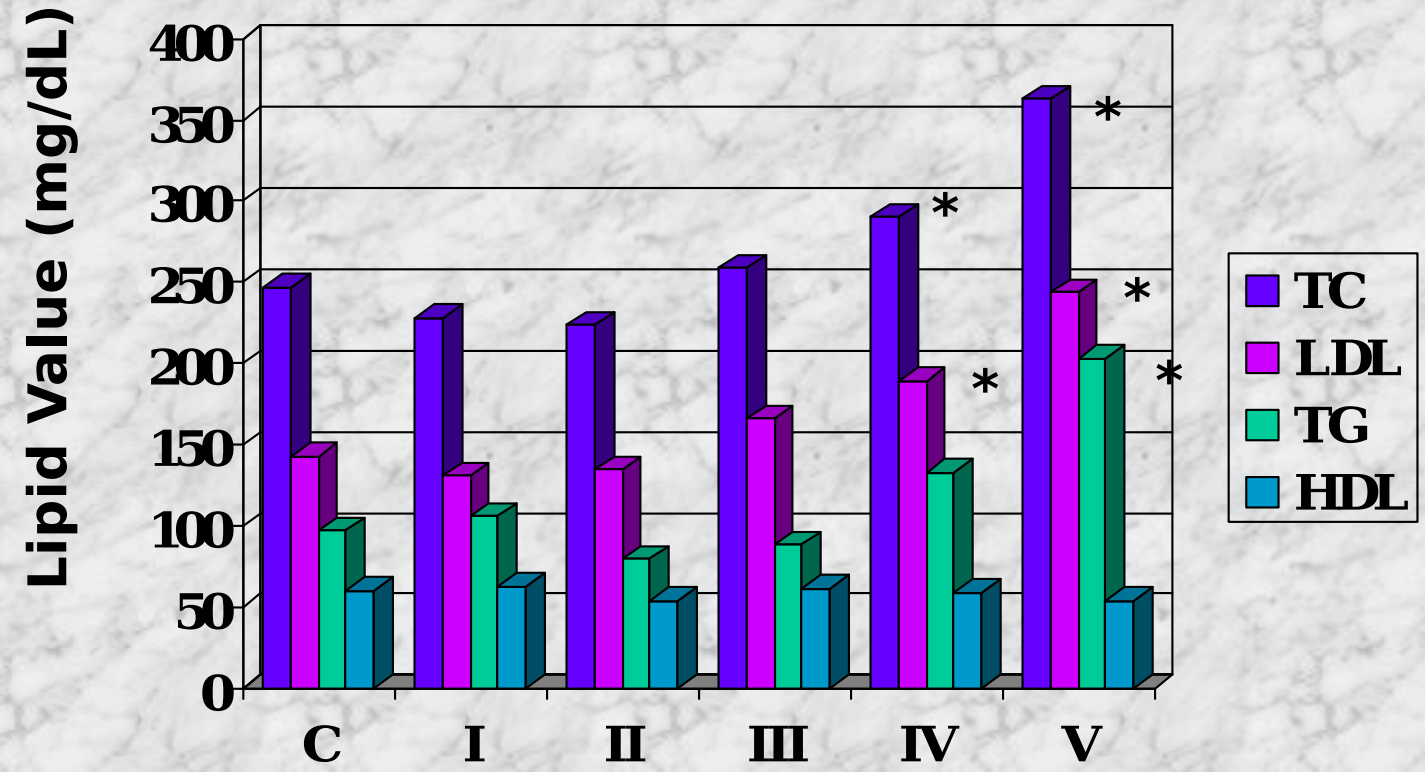
Hyperlipidemia in Hypothyroidism: Patterns



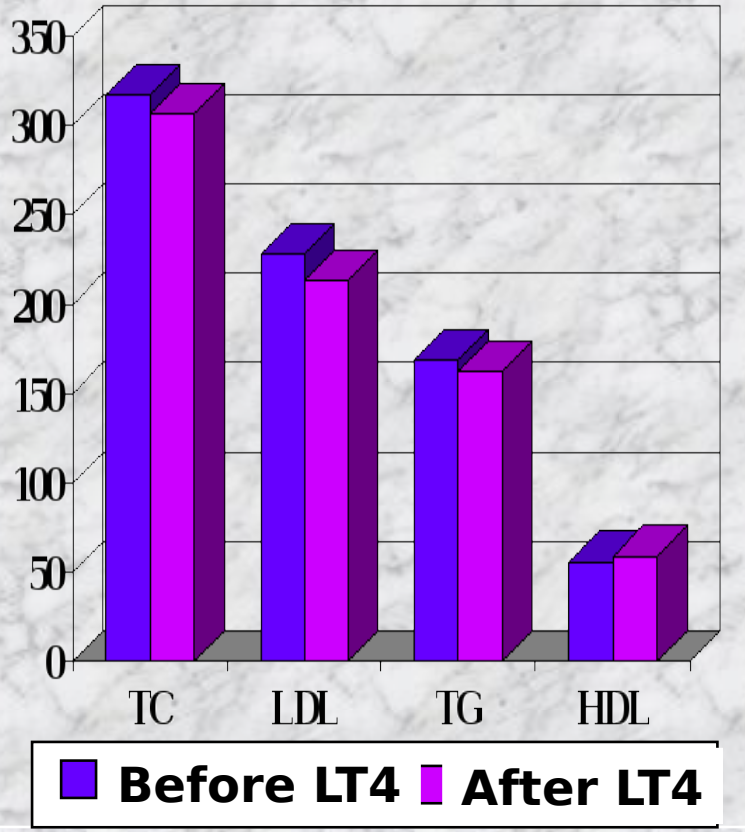
ANOVA: TC, LDL, TG: P < 0.001 vs. control; HDL ns

Staub Am J Med 1992; 92:63

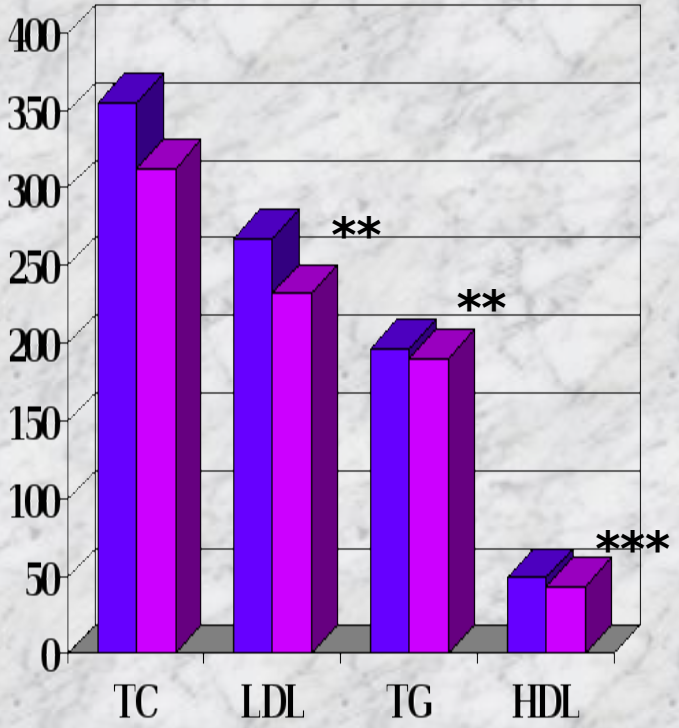
Subclinical Hypothyroidism: Effect of Thyroxine on Lipids

21 Patients selected from referrals to a lipid clinic

TSH 5.0-9.9 mU/L(n=6)



TSH 10.0-39.9 mU/L (n=8)



***p < 0.05; **p < 0.02; ***p < 0.01**

Diekman et al. Arch Intern Med 1995; 155:1490

Case #1: 64-Year-Old Female

- Levothyroxine started 0.05 mg/d increased to 0.1 mg/d
- TFTs: TSH 1.5
- BP 114/72
- Lipids: Tchol 185, HDL 55, LDL 102
- Diltiazem dose reduced, pravstatin discontinued

Case #2: 69-Year-Old Male

- Chief complaint: sweating, decreased energy, HA, decreased libido, diminished visual acuity all over 2 years
- PMH: CAD s/p CABG x3, gout,↑ lipids
- FH: negative
- Rx: Nitrobid, lopid, ECASA

Case #2: 69-Year-Old Male

Physical exam

- BP 114/68 Pulse 60
- Neck: no goiter
- Chest: ? Gynecomastia
- GU: Atropic testes (15 cc) bilaterally
- DTRS: Decreased relaxation phase

Case #2: 69-Year-Old Male

Laboratory

- CBC: WBC 4.5, Hct 33.5 %, PLT 206 K
- Lytes Na+ 142, K+ 4.5
- FT4 7.7 pmol/ L (normal10.3-30.6 pmol/L)
- TSH 0.37 (normal 0.5-5.0 mIU/L)

Case #2: 69-Year-Old Male

Interim Questions

- What are the possible causes of his thyroid function test abnormality?

Case #2: 69-Year-Old Male

Interim Questions

- What are the possible causes of his thyroid function test abnormality?
  - T3 thyrotoxicosis
  - Recovery from thyroiditis
  - Central hypothyroidism

Case #2: 69-Year-Old Male

Interim Questions

- What further evaluation would you do?

Case #2: 69-Year-Old Male

Endocrine evaluation

- Repeat TFTs: identical pattern
- Free T3 2.7 (1.5-6.9 pmol/L)
- Prolactin 4.3 ng/mL (normal 2.7-16.8)
- GH < 1.0 (0.06-5.0 ng/mL); SmC 25.5 (71-290)
- LH 1.4 ↓ (2.4-9.4 mIU/mL)
- FSH 4.0 (0.9-15.0 mIU/mL)
- Free Testosteone ↓ 1.4 (5.1-41.0 ng/dL)
- Basal cortisol 3.3 ug/dL→10.6 (30') → 12.6 (60')

Case #2: 69-Year-Old Male

Endocrine evaluation (cont'd):

- MRI sella:
  - 2.5 cm pituitary adenoma with invasion bilaterally into cavernous sinus and compression of the optic chiasm
- VF-bitemporal hemianopsia

Case #2: 69-Year-Old Male

Follow-up

- Patient underwent TSS for nonfunctional pituitary adenoma resection; VF improved.
- Patient started on hydrocortisone, thyroid hormone, and testosterone replacement therapy. Energy level and libido normalized
- Labs: Hct 41%, FT4 20.0 pmol/L, TSH 0.24 mIU/L.

Case #2: 69-Year-Old Male

Final Questions:

- How would you interpret his current TFT results (FT4 20.0 pmol/L, TSH 0.24)?
- What were the clues to a central etiology for his hypothyroidism?
  - Sxs?
  - Signs?
  - Labs?

Case #2: Clues to Central Hypothyroidism

- Sxs: HA, decreased libido, sweats (?T-def), visual changes
- Signs: (-) goiter (why not?); (+) gynecomastia; (+) atrophic testes
- Labs: nc/nc anemia, tft pattern, secondary hypogonadism pattern, low cortisol level

Case #3 37-Year Old Female

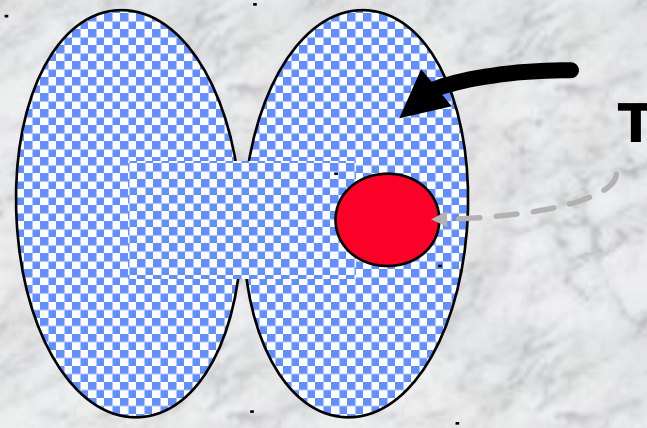
- Pt c/o 2 mo Hx neck swelling
- No hoarseness, neck pain, dysphagia, or history of neck irradiation
- Pt had a thyroid scan and US, the findings of which prompted referral

Case #3 37-Year Old Female

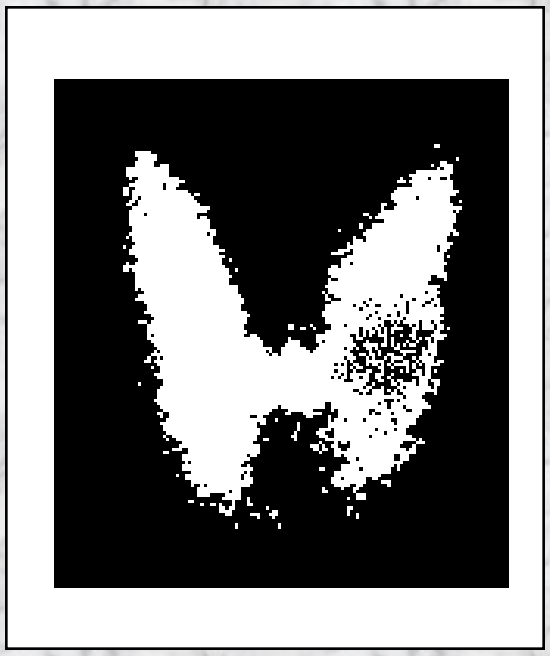
- Labs: FT4 17.2 (10-20 pmol/L)
- TSH 1.2 mIU/L
- US: 1.7 x 1.7 cm partially cystic right thyroid nodule; 0.5 cm nodule on left
- Thyroid scan: cold defect in RML
- FNA thyroid: colloid, macrophages, microfragments of follicular cells, c/w nodular goiter

Case #3 37-Year Old Female

THYROID SCANNING WITH 99m-Tc



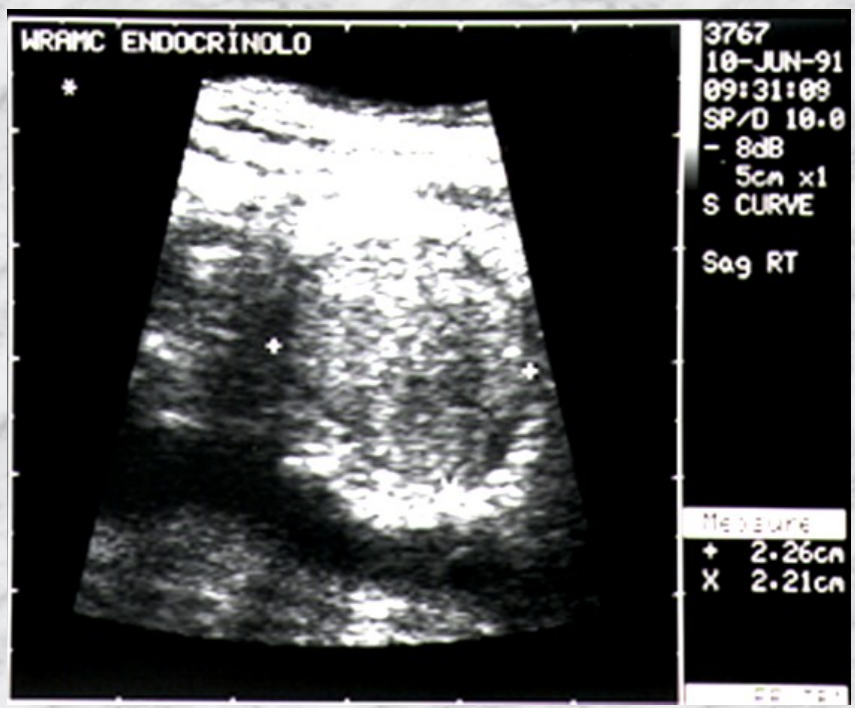
Thyroid “traps” Tc-99m



Case #3 37-Year Old Female

THYROID ULTRASOUND

- **Thyroid vs. nonthyroid**
- **Document size of nodule**
- **Solitary vs. multinodular**



Case #3 37-Year Old Female

Course

- Patient was given a trial of LT4 suppression
- Despite TSH suppression, US showed no change in nodule over a 6 mo period.
- Repeat FNA: hypercellular specimen w/ nuclear atypia suggestive of papillary thyroid cancer
- Referred for thyroidectomy followed by I-131

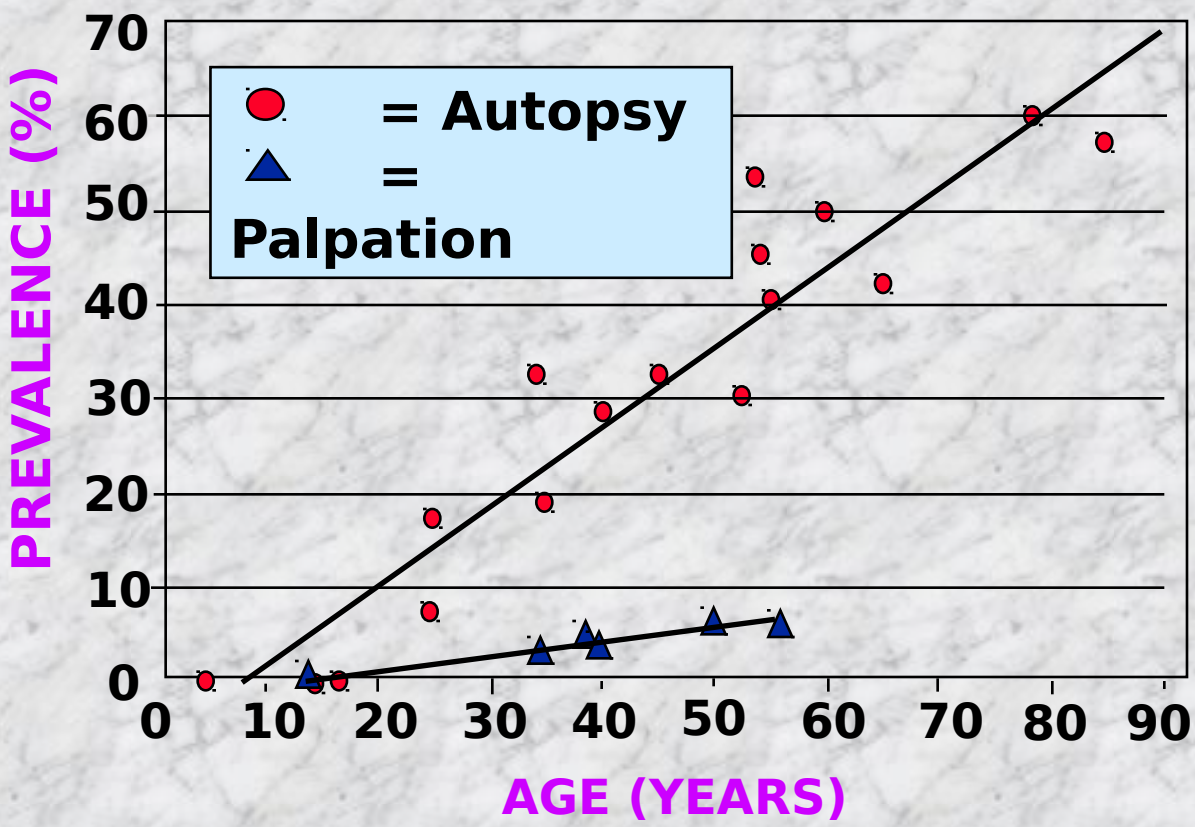
Case #3 37-Year Old Female

Question:

- What is the prevalence of thyroid nodules in the general population?

Prevalence of Thyroid Nodules:

The Effect of Age



Mazzaferri. N Engl J Med 1993;328:5

Case #3 37-Year Old Female

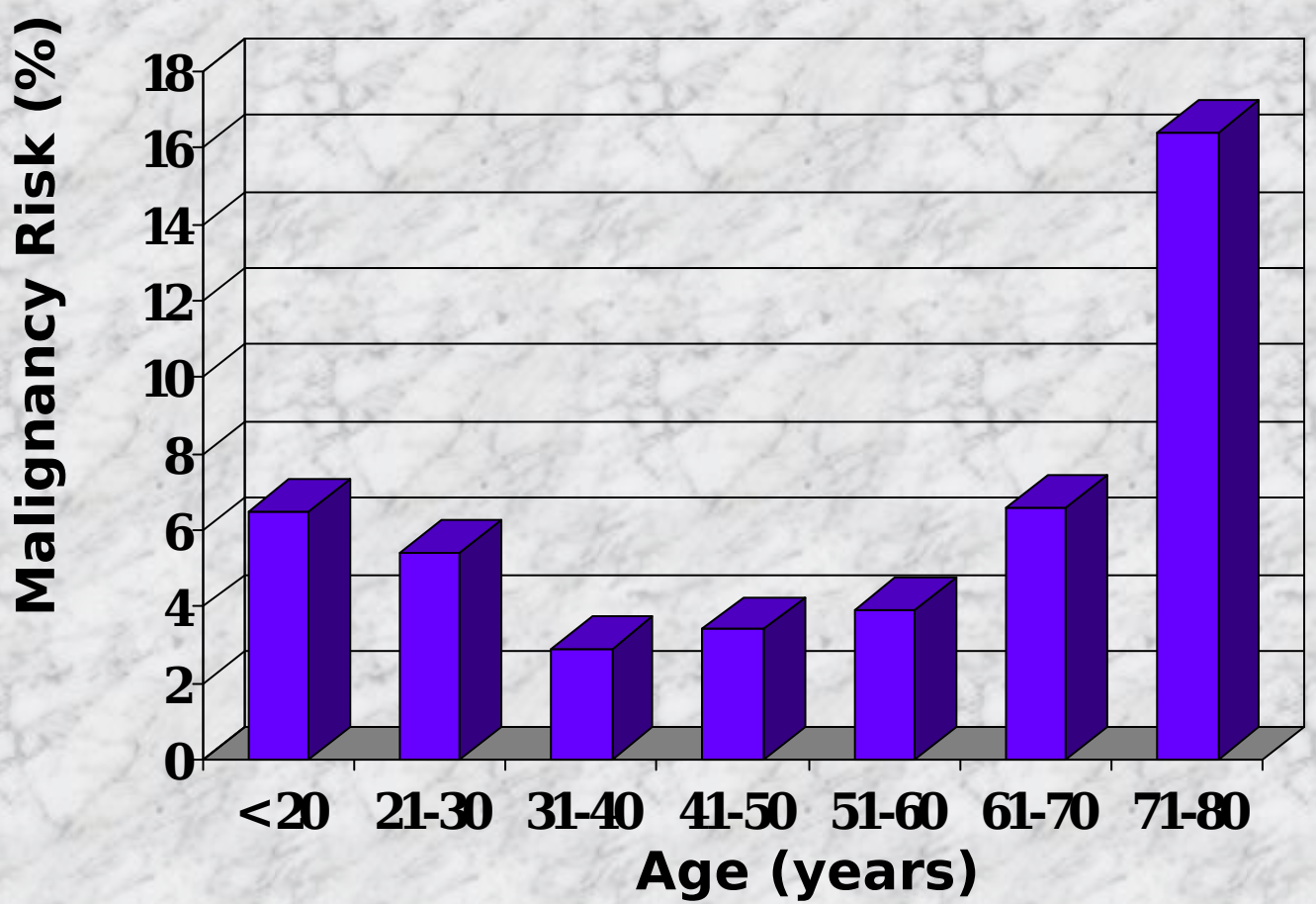
Question

- How do the following factors influence the risk that a thyroid nodule is malignant?
  - Patient age and gender?
  - Hx of childhood neck irradiation?
  - MNG vs. solitary
  - Cystic change on US?
  - Lack of nodule shrinkage on thyroid hormone?
  - Benign FNA results

The Effect of Age and Gender on Thyroid Nodule Cancer Risk

- **Extremes of age: higher risk**
  - **Age 20 or less**
  - **Males over 60**
- **Effect of Gender**
  - **Nodules more common in women, but... cancer within nodule more likely in men**

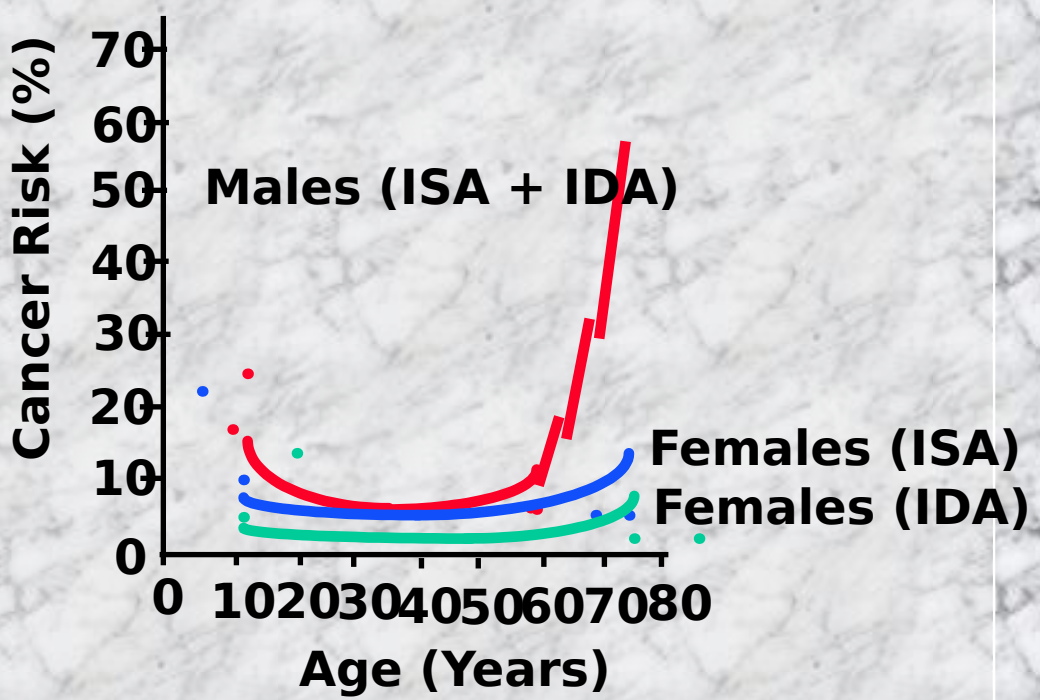
Thyroid Nodule Cancer Risk by Age



Belfiore et al Am J Med 1992;93:3

Thyroid Nodule Cancer Risk by Gender

- **5,637 patients with “cold” thyroid nodules**
- **792 referred for surgery**
- **Cancer rates compared in males, females, by age**



Belfiore et al Am J Med 1992;93:36

The Effect of Thyroid Irradiation

- **Neck irradiation widely used in the 1950-60's**
- **Conditions treated: enlarged thymus, tonsils and adenoids, acne, tinea capitus, impetigo, sinusitis, pertussis, keloid, and Bell's palsy.**
- **Approximately 1/3 develop thyroid nodules**
- **1/3 of these have thyroid cancer**
- **Peak incidence 15-30 years after XRT**
- **Women higher risk than men after XRT**

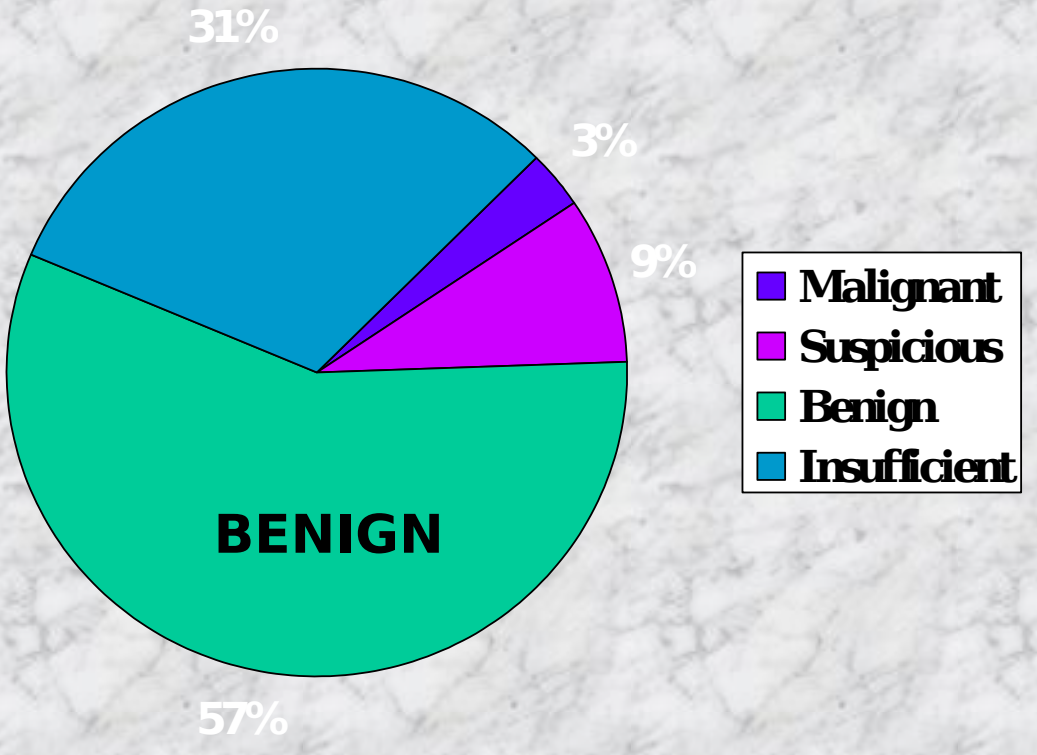
Case #3 37-Year Old Female

Question

- How do the following factors influence the risk that a thyroid nodule is malignant?
  - Patient age and gender?
  - Hx of childhood neck irradiation?
  - MNG or cystic change on US?
  - Lack of nodule shrinkage on thyroid hormone?
  - Benign FNA results

Thyroid FNA Results at WRAMC

DISTRIBUTION OF RESULTS:

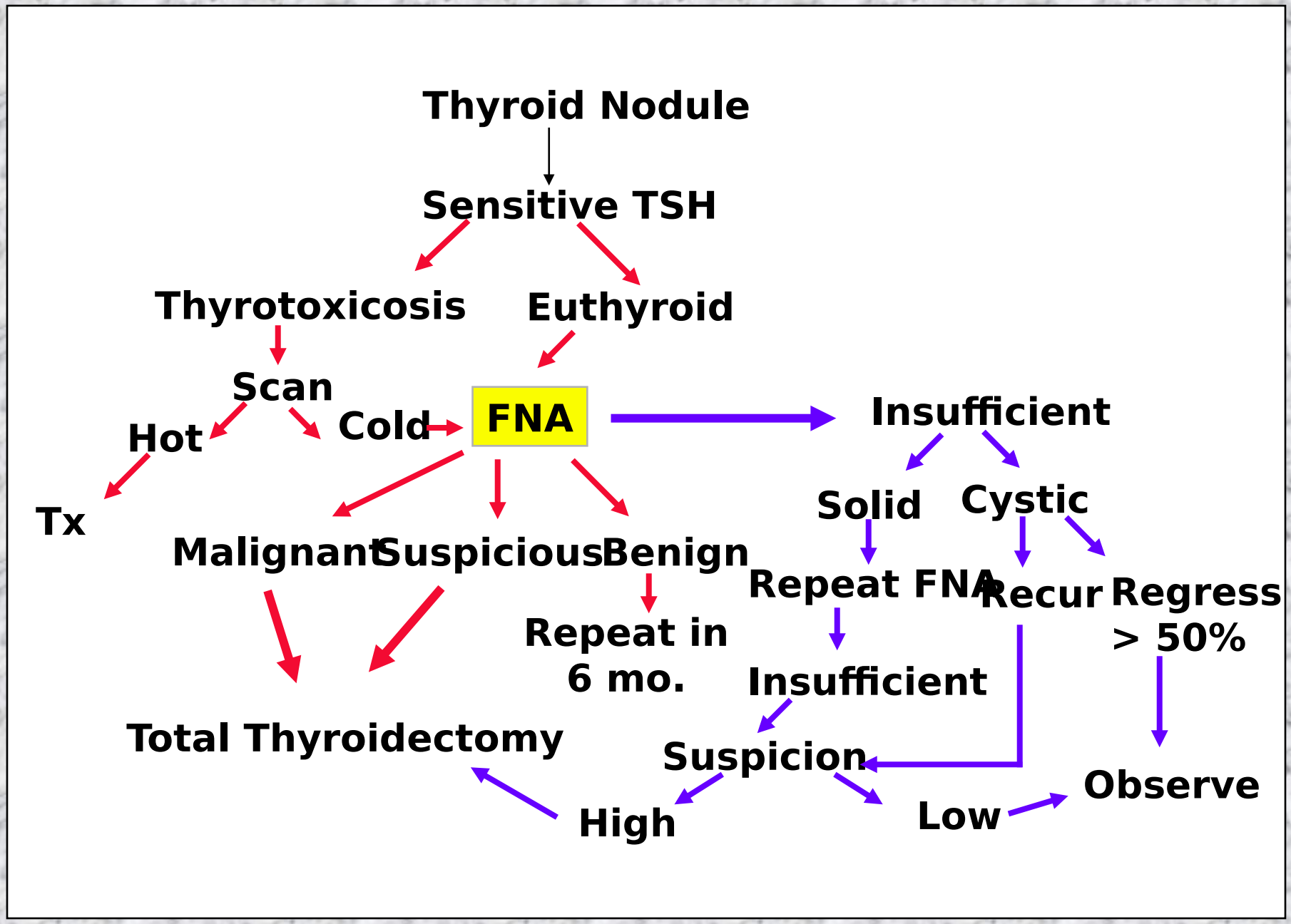


Burch et al. Acta Cytologica 1996; 40:1176-83

Case #3 37-Year Old Female

Question

- What is the most efficient, cost effective approach to evaluating thyroid nodules?



Burch HB, Endocrin Metab Clin North Am 1995;24:663.

Case #4: 39-Year-Old Female

- Pt noted lump in neck 12/98, observed x 2 months before seeking medical attention
- PMHx: no XRT to neck, no HTN, no kidney stones
- FH: no thyroid disease Hx in parents, sibling, children
- PE: Pulse 88 BP 135/84; Neck: 2.5 cm thyroid nodule on right, no LN.

Case #4: 39-Year-Old Female

- FNA of nodule: c/w Hürthle cell neoplasm
- Total thyroidectomy
- Pathology: bilateral medullary thyroid cancer
- Post-op calcitonin testing: undetectable

Case #4: 39-Year-Old Female

Questions

- What are the types and distribution of thyroid cancer?
- What further testing is required?
  - In this patient?
    - Immediately
    - Long-term surveillance
  - In her family members?

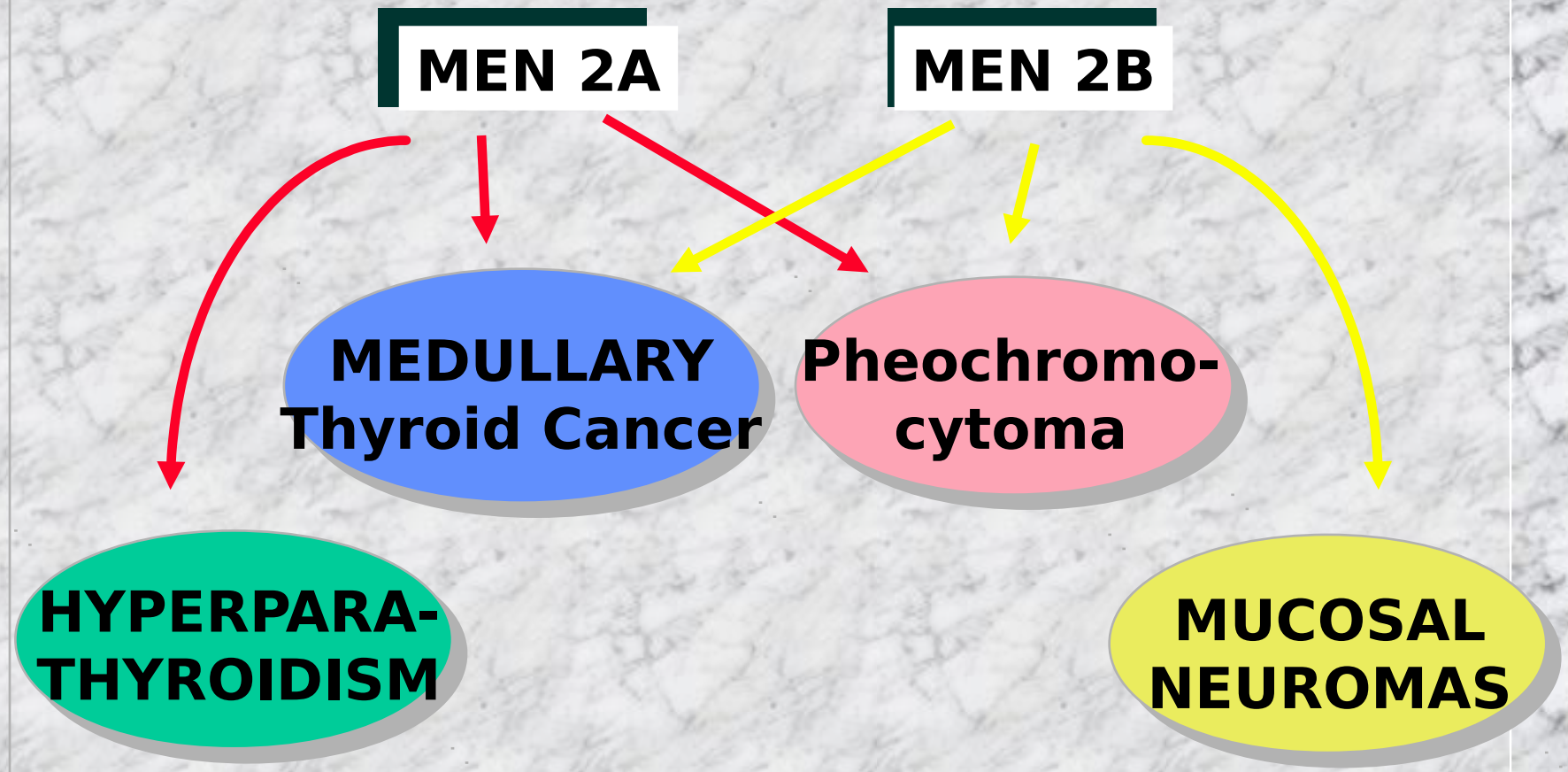
Types and Distribution of Thyroid Cancer Cases

- **Papillary** **70-80%**
- **Follicular** **10-15%**
- **Medullary** **5-10%**
- **Anaplastic** **5%**

Case #4: 39-Year-Old Female

- Classification of Medullary Thyroid Cancer
  - Sporadic
  - Familial
    - MEN-2A
    - MEN-2B
    - Non-MEN
- Effect on Prognosis
  - Familial non-MEN (best) > MEN 2A > Sporadic > MEN 2B (worst)

MEN Syndromes and Thyroid Cancer



Case #4: 39-Year-Old Female

- Further testing: patient
  - Screen for hyperparathyroidism (30% MEN 2A)
  - Screen for pheochromocytoma (50% MEN 2 pts)
  - RET protooncogene activating mutation
    - MEN 2A & Non-MEN FMTC: 95% (exon 10-11)
    - MEN 2B: 90% (exon 16)
    - Sporadic: 25-65% (exon 16)

Case #4: 39-Year-Old Female

- Further testing: family members
  - RET protooncogene mutation if patient (+)
  - If patient RET mutation negative, other means of screening families have been utilized including Calcium/ pentagastrin stimulation testing, genetic linkage analysis.

Case #4: 39-Year-Old Female

Follow-up

Testing results: patient

- RET (+) at AA 634 (common site for MEN 2A)
- Negative screen for pheochromocytoma, hyperparathyroidism

Testing results: family

- Children RET (-), sibling & parents refused testing

Questions?